A Splicing Modulator Targeting Cancer Stem Cells in Acute Myeloid Leukemia

Grant Award Details

A Splicing Modulator Targeting Cancer Stem Cells in Acute Myeloid Leukemia

Grant Type: Therapeutic Translational Research Projects

Grant Number: TRAN1-10540

Investigator:

Name:	Catriona Jamieson
Institution:	University of California, San Diego
Type:	PI

Disease Focus: Acute Myeloid Leukemia, Blood Cancer

Award Value: $2,700,420

Status: Pre-Active

Grant Application Details

Application Title: A Splicing Modulator Targeting Cancer Stem Cells in Acute Myeloid Leukemia

Public Abstract:

Translational Candidate

17S-FD-895 is a potent small molecule splicing modulator that inhibits aberrant splicing in CSCs that have deregulated SF3B1 expression.

Area of Impact

Development of 17S-FD-895 could address a major bottleneck to reducing AML mortality by targeting splicing deregulated-CSCs that fuel AML relapse.

Mechanism of Action

17S-FD-895 will positively impact patients with AML by providing a potent and selective CSC-targeted therapeutic strategy that could prevent relapse and improve overall survival. In addition, splice isoform biomarkers of CSC response to 17S-FD-895 have already been identified. Through targeted modulation of the RNA splicing machinery, we can alter and monitor the splicing response to 17S-FD-895, which provides a vital companion diagnostic for proof-of-concept studies in future clinical trials.

Unmet Medical Need

Despite recent advances in molecular targeted and immunotherapeutic strategies, patients with AML have a 5 year life expectancy of only 26% due to high relapse rates fueled by CSCs. CSCs are uniquely sensitive to splicing modulation and can be selectively inhibited by 17S-FD-895.

Project Objective

Pre-IND meeting

Major Proposed Activities

- Manufacture sufficient quantities of 17S-FD-895 to complete key pre-IND studies
- Complete non-clinical safety and toxicology studies, pre-clinical studies and biomarker testing as proof-of-concept for future clinical applications
- Complete pre-IND studies and have a pre-IND meeting

Statement of Benefit to California:

For nearly 50 years, no therapies have significantly reduced relapse-related mortality in acute myeloid leukemia (AML). The rapid lethality of AML relapse is underscored by the fact that in California in 2014 there were 1,112 deaths from AML and 1,614 new patients diagnosed. A selective cancer stem cell-targeted agent, 17S-FD-895, offers a novel therapeutic candidate for AML patients and those suffering from other recalcitrant cancers, providing hope for many of our fellow Californians.

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